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Sleep problems and cognitive behavior therapy in pediatric obsessive-compulsive disorder have bidirectional effects

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ABSTRACT

Objectives: To investigate the presence of sleep problems and their reaction to CBT in pediatric obsessive compulsive disorder (OCD). Moreover, we investigated whether sleep problems predict the outcome of CBT on OCD-symptoms.
Methods: 269 children and adolescents, age 7–17 years, with DSM-IV primary OCD that took part in the first step of a stepwise treatment trial, were assessed with regard to both individual sleep problems and a sleep composite score (SCS) using the Child Behavior Checklist (CBCL). Their OCD symptoms were rated using the Children Yale-Brown Obsessive Compulsive Scale (CY-BOCS).
Results: We found elevated symptoms of sleep deprivation and nightmares before treatment. However most sleep problems (e.g. nightmares ($p = .03$), too little sleep ($p < .001$), trouble sleeping ($p < .001$) and parasomnias $p = .03$)) as well as being over-tired ($p < .001$) reduced during CBT treatment. Co-morbidities had no effect on the reduction of SCS. Moreover, elevated levels of sleep problems using the SCS ($p < .001$), as well as any sleep problem at baseline ($p < .001$) predicted less effect of CBT on the OCD symptoms.
Conclusion: Sleep problems in paediatric OCD are frequent and interfere with treatment outcome. They need to be assessed using better methods in future trials. Moreover, lack of resolution of sleep problems need to be recognized and treated as it seems probable that continued sleep problems may have a negative impact on CBT efficacy.

1. Introduction

Sleep problems are common in both children and adolescents and have been reported among young people in the range 10–75% (assessment methods have varied). Moreover, the difficulties seem to persist in many, although decreasing with age in many as well (Gregory, Rijsdijk, Dahl, McGuffin, & Eley, 2006; Zuckerman, Stevenson, & Bailey, 1987). However, childhood sleep problems may persist into adolescence (Gregory & O'Connor, 2002).

Continued sleep problems are associated with psychiatric disorders (Chorney, Detweiler, Morris, & Kuhn, 2008; Gregory & Sadeh, 2012; Ivanenko & Johnson, 2008). In anxiety disorders and depression, sleep problems are especially common (Alfano, Beidel, Turner, & Lewin, 2006; Alfano, Ginsburg, & Kingery, 2007; Charuvastra & Cloitre, 2009; Chase & Pincus, 2011; Hudson, Gradisar, Gamble, Schniering, & Rebelo, 2009; Ivanenko, Crabtree, & Gozal, 2004), less than 1 in 10 reported, for example, no problems (Chase & Pincus, 2011). Such problems are essential parts of the disorder in generalized anxiety and depression (American Psychiatric Association, 2013). However, other psychiatric disorder with high levels of anxiety, e.g. OCD, is also strongly associated with sleep problems (Dubitsky, 2005; Ivarsson & Larsson, 2009), as are ADHD (Cortese et al., 2013) and autism (Goldman, Richdale, Clemons, & Malow, 2012).

In paediatric anxiety disorders and OCD, studies using sleep assessment methods have clarified that sleep problems are both prevalent and specific (Alfano & Kim 2011; Alfano, Pina, Zerr, & Villalta, 2010; Alfano, Reynolds, Scott, Dahl, & Mellman, 2013; Alfano, Zakem, Costa, Taylor, & Weems, 2009; Forbes et al., 2008). That is, that the sleep problems are not a halo effect from the disorder, or due to a lack of specificity in assessment methods.

Abbreviations: OCD, obsessive-compulsive disorder; PDD NOS, pervasive developmental disorder not otherwise specified; ADHD, attention deficit hyperactivity disorder; CBT, cognitive behavior therapy; SRI, serotonine re-uptake inhibitor; SSRI, specific SRI; NordLOTS, Nordic Long-term OCD Treatment Study; KSADS, Kiddie schedule for affective disorders and schizophrenia; CY-BOCS, Children's Yale-Brown Obsessive Compulsive Scale; CBCL, Child Behavior Check List; CGI, Clinical Global Impression; LME, linear mixed effects model; POTS, Pediatric OCD Treatment Study.

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Clinical experience shows that obsessive ruminations with elevated levels of anxiety and arousal before bedtime as well as rituals that delay sleep onset are common in paediatric OCD, even though research did not show increased latency to sleep (Alfano & Kim, 2011). However, residual arousal leading to more shallow sleep, and difficulties in falling asleep again following awakening may cause the fragmented sleep pattern noted by Alfano and Kim (2011). Although, it is difficult to explain the link between too little sleep and more severe compulsive behaviours it is possible that different rituals (e.g. mental rituals bed) may be responsible. This relationship needs to be replicated. Few studies have examined sleep problems in paediatric OCD, two studies using large samples (Ivarsson & Larsson, 2009; Storch et al., 2008), showed that such problems were prevalent, in that, about a third had significant problems, and that less than 10% had none. However, the assessment methods used were unspecific (CBCL – depression and anxiety scales sleep items). The findings are substantiated by a study using sleep specific assessment methods in a smaller sample, showing that sleep problems are both common and severe (Alfano & Kim, 2011). She found that the patients' sleep patterns were fragmented, that the total sleep time was reduced and that patients spent longer wake periods after sleep onset as compared to controls. Moreover, the severity of compulsions but not obsessions was significantly related to total sleep time (TST), indicating less TST among children with elevated compulsions.

However, there is still little data as to whether sleep problems associated with OCD reduce from treatment, and whether it is common with residual significant sleep problems in responders or non-responders to treatment. Storch et al. (2008) found a significant reduction of sleep problems following cognitive behaviour therapy (CBT) for OCD. However, we are not aware of any studies showing whether serotonin re-uptake-inhibiting (SRI) agents for OCD reduce sleep problems as well. Moreover, we as well lack data on whether sleep problems may compromise treatment with CBT.

2. Aims

To investigate the presence of sleep problems in the Nordic Long-Term OCD Treatment Study (NordLOTS) (Torp et al., 2015) and to what extent sleep was affected by CBT for the OCD-symptoms. Furthermore, to investigate whether sleep problems at baseline were associated with poorer response of CBT.

3. Methods

The data are part of the NordLOTS, a stepwise treatment study aiming at evaluating whether CBT or drug treatment with sertraline is best for children and adolescents with OCD who do not respond to CBT. The rationale, design and methods of the NordLOTS are described elsewhere (Ivarsson et al., 2010; Thomsen et al., 2013). In short, it started in September 2008 and finished inclusion in June 2012, when a large cohort of patients with OCD ($n = 269$) their first treatment step with 14 weeks of CBT in three countries, and five sites using 19 clinics.

3.1. Participants

We assessed and treated 269 pediatric patients in the study, with patients recruited through community mental health centres, general practitioners, child mental health specialists and parents/relatives. Inclusion criteria into step 1 of the study were: (1) a primary diagnosis of OCD in accordance with the criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), Text Revision (American Psychiatric Association, 2000); (2) moderate to severe OCD (CY-BOCS entry score ≥ 16); (3) being from 7 to 17 years of age. Exclusion criteria were kept to a minimum, in order to ensure a representative sample of paediatric patients seeking treatment for OCD. These included: (1) the presence of a DSM-IV psychiatric disorder with a higher treatment priority (i.e. psychosis and severe depression); (2) mental retardation and/or autism spectrum disorders (a diagnosis of PDD NOS was allowed as long as OCD was judged to be the principle disorder based on the respective Clinical Global Impression-Severity (CGI) scores); (3) a previous failed trial of E/RP for OCD within less than 6 months prior to inclusion; (4) medication treatment with SRI less than 6 months prior to inclusion; and (5) inadequate language proficiency by the patient or the parent.

3.2. Measures

The OCD and co-morbidity diagnosis was made using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) (Kaufman et al., 1997). It is a semi-structured diagnostic interview that assesses a range of child psychopathology, and has good psychometric properties e.g. an inter-rater reliability of 98% and a 1–5 week test-retest kappa of .80 for any anxiety disorder diagnosis. Good convergent and divergent validity have been shown in a Nordic sample of adolescents (Lauth et al., 2010). In this report, we use only diagnoses at a group level, e.g. any depressive disorder, any anxiety disorder, any ADHD, and any tic disorder. Data on the co-morbidity can be found in a previous paper from our group (Torp et al., 2015).

The Children Yale-Brown Obsessive Compulsive Scale (CY-BOCS) (Goodman et al., 1989) is a clinician-rated, semi-structured interview assessing the character and severity of OCD symptomatology. It uses ten severity items across five dimensions (time occupied by symptoms, interference, distress, resistance and degree of control over symptoms for obsessions and compulsions separately, yielding a total severity score from 0 to 40. The CY-BOCS shows reasonable reliability and validity (Gallant et al., 2008; Scahill, Riddle, McSwiggin-Hardin, & Ort 1997; Storch et al., 2004).

The Child Behavior Checklist (CBCL) (Achenbach & Rescorla, 2001) is a wide spectrum symptom assessment tool which allows parents to rate their children's psychological and psychiatric symptoms. It also contains six items assessing sleep problems: "experiences nightmares," "sleeps less than most children," "sleeps more than most children," "talks or walks in sleep," "trouble sleeping," and "overtired". A "sleep problem scale" has been used that adds scores on these six items. This general sleep problem scale has been used in previous research (e.g. (Alfano, Ginsburg, & Kingery, 2007; Gregory & O'Connor, 2002; Stoleru, Nottelmann, Belmont, & Ronsaville, 1997) and it yields a score from 0 to 12. The internal consistency of the scale was higher than in the previous study of Gregory (2002), or $\alpha = .64$. However, no specific sleep scale was included in the assessments so that, for example, the assessment of the circadian rhythm, sleep latency or total sleep time was not examined.

3.3. Treatment

All participants were treated with exposure-based CBT based on a published manual used in previous treatment outcome studies (March & Mulle, 1998; POTS Treatment Study Team, 2004). The manual was modified by adding more extensive family participation based on the work of Piacentini et al. (2011). All details can be found in Torp et al. (2015) and Thomsen et al. (2013). Briefly, the treatment consisted of 75 min weekly sessions for 14 weeks. Parents were expected to accompany their children to all sessions. The children were seen together with their parents in 6 of the 14 sessions (sessions 1–3, 5, 11, and 14). In the remaining sessions, the child was treated individually for 45 min and then the parents were

seen with or without the child for an additional 30 min. This extra time was added specifically to address issues regarding the parents' involvement in therapy, and their attitude and feelings about their child's OCD symptoms. There were no interventions that were specifically directed toward sleep problems. However, obsessions and compulsions that interfered with sleep were addressed. For instance, obsessions and anxiety that interfered with sleep by causing arousal or time-consuming rituals interfering with sleep.

3.4. Statistical analyses

We used the non-parametric homogeneity test for investigating the change of individual sleep problems across the treatment period. Moreover, the exact χ^2 test was used to test for the association of independent categorical factors.

The sleep scale score was obtained by calculating the sum score of the six sleep-related CBCL items. To obtain a sum score for as many participants as possible we allowed one item to be missing. Moreover, we used linear mixed models (LME) (Fitzmaurice, 2011; Gueorguieva & Krystal, 2004) (1) to investigate how sleep problems as a global construct changed following treatment. Fixed effects were time (baseline, week 7 and week 13). (2) We investigated whether OCD symptoms at baseline and the presence of comorbid disorders predicted poorer outcome of the sleep problem scale after treatment with separate LMEs. The models included fixed effects for time, predictor and their interaction. Third, we investigated whether the sleep problem scale predicted poorer treatment outcome (reduction of OCD symptoms measured by the CY-BOCS). Fixed effects were weeks from baseline, the sleep problem scale and their interaction. In all models, random effects included intercept and linear slope terms. Simulation studies have shown that linear mixed-effects models perform similarly to multiple imputation in terms of dealing with missing data in the dependent variable (Peters et al., 2012), thus no multiple imputation was done prior to the linear mixed-effects analysis. An unstructured covariance was used in order to account for within patient correlation across time. Tests were two-tailed, and a p-value of less than .05 was considered to indicate statistical significance. All analyses except the LMEs were performed by SPSS version 21.0. The LMEs were performed using the PROC MIXED procedure within the SAS Statistical Software, version 9.3. The with-in group effect size was computed as described by Morris & DeShon (2002).

As would be expected in a symptom count measure of psychopathology, the CBCL derived sleep scale used in the analyses was skewed. Accordingly, we transformed the data using a log transform. Although all analyses are performed on normalized log transformed data, descriptive findings are reported as raw (untransformed) data.

4. Results

4.1. Demographics

There were no gender differences with regard to sleep problems (Girls $m = 2.09$, SD = 1.98 and Boys $m = 1.96$, SD = 2.40, $p = .63$), nor any age differences (7–11 years $m = 2.23$, SD = 2.34 and 12–18 years $m = 1.94$, SD = 2.12, $p = .33$). When examined with regard to the frequency of individual sleep problems both differences with regard to gender and age group (children vs. adolescents) were not significant, so we did not use age or gender as covariates.

4.2. Baseline prevalence of sleep problems

68.3% ($n = 168$) of children had at least one mild sleep problem. However, sleep problems scored as present often or to a high degree were quite common as well (26.8%, $n = 66$) and 14.2% ($n = 35$) had two or more problems scored as often/to a high degree. Indeed, more than one out of four had a frequent or severe sleep problem. Individual sleep problems before and after treatment are to be found in Table 1. The most common problems (endorsed as somewhat or sometimes true and very true or often true) were in this order "trouble sleeping (40%), nightmares (33.2%), sleeps less (29.5%), overtired (26.2%). "talks or walks in sleep" (16.2%) and sleeps more (9.5) occurred more seldom.

4.3. Outcome

All individual sleep problem except "sleeps more than other kids" reduced following CBT (Table 1).

Moreover, what could be seen as a negative consequence of disordered sleeping, "Overtired without good reason", that was present in one quarter of the participants at baseline reduced significantly as well.

Two forms of sleep problems were uncommon among our patients: "Sleeps more than most kids" and "talks or walks in sleep". "Sleeps more than most kids" did not reduce significantly across time, which "talks or walks in sleep" did (Table 1).

Patients who did not respond to CBT (CY-BOCS scores following treatment were 16 or higher) had at least one persistent severe/frequent sleep problem (19.2%), something which was less common in CBT responders (6.9%) ($\chi^2(1197) = 6.383$, $p = .012$). However, sleep problems were still common, as a majority had at least one residual mild/infrequent or severe sleep problem in both groups (responders 46.9% and non-responders 65.4%, $\chi^2(1197) = 5.525$, $p = .022$), while only 34.6% of responders and 53.1% of the non-responders had no sleep problems at all. The change in the degree of sleep problems on the composite sleep scale from baseline to week 13 was significant ($p < .001$) showing that sleep problems reduced during these 13 weeks. The estimated score at baseline was 2.03 (95% CI 1.80–2.27) and it decreased to 1.02 (95% CI 0.76–1.27) at week 13. The with-in group effect size was 0.51 (95% CI 0.33–0.69).

4.4. Predictors of sleep change

OCD symptoms at baseline (CY-BOCS total score) did not predict changes in sleep problems ($p = .549$).

Furthermore, the presence of co-morbid anxiety disorders, any depressive disorders, ADHD and tic disorders were evaluated with regard to its effect on the reduction of sleep problems.

Anxiety disorders did not predict changes in sleep problems through treatment ($p = .375$). Children with comorbid anxiety disorders had more sleep problems before ($p < .001$) as well as following treatment with CBT ($p = .007$). Moreover, ADHD predicted change in sleep problems ($p = .038$), children with ADHD had more sleep problem at baseline ($p < .001$) but there was no difference between groups at post-treatment ($p = .325$). The presence of tic disorders did not predict change in sleep problems ($p = .554$). No difference was found between children with or without comorbid tic disorders at baseline ($p = .228$) or at post-treatment ($p = .602$). Furthermore, there was a marginally significant trend ($p = .078$) for co-morbid depressive disorders to predict changes in sleep problems. Although no differences were found between children with or without depressive disorders at baseline ($p = .424$) or at post-treatment ($p = .267$), the direction of the trend was that non-depressive children scored higher on the scale at baseline (Hedges $g = -0.27$, 95% CI −0.91 to 0.36) but the depressive children scored higher at the end of the treatment (Hedges $g = 0.41$, 95% CI −0.22 to 1.05).

Table 1
Sleep problems before and following treatment with CBT.

	Baseline	Following CBT				Marginal homogeneity test
		Not true	Somewhat or sometimes true	Very true or often true	Missing	
Nightmares	Not true	117	12	0	36	$p < .001$
	Somewhat or Sometimes true	33	21	0	15	
	Very true or often true	2	8	1	2	
	Missing	6	0	0	16	
Overtired without good reason	Not true	139	6	0	38	$p < .001$
	Somewhat or sometimes true	19	10	3	12	
	Very true or often true	10	6	2	3	
	Missing	6	0	0	15	
Sleeps less than most kids	Not true	122	7	1	42	$p < .001$
	Somewhat or sometimes true	26	14	2	8	
	Very true or often true	5	8	3	6	
	Missing	7	1	1	16	
Sleeps more than most kids	Not true	170	3	1	47	$p = .17$
	Somewhat or sometimes true	4	4	0	8	
	Very true or often true	4	1	0	2	
	Missing	10	0	0	15	
Talks or walks in sleep	Not true	150	6	0	46	$p = .03$
	Somewhat or sometimes true	15	9	1	10	
	Very true or often true	2	1	0	1	
	Missing	12	1	0	15	
Trouble sleeping	Not true	96	6	4	41	$p < .001$
	Somewhat or sometimes true	30	9	1	8	
	Very true or often true	22	10	8	10	
	Missing	5	3	1	15	

4.5. Sleep problems as a possible predictor of CBT response

We used LME to investigate whether sleep problems were associated with poorer treatment outcome measured by the CY-BOCS. The sleep problem scale predicted CBT response ($p < .001$). Furthermore, the sleep problem scale was dichotomized, so children who had no sleep problems (a score of 0 on the scale) (31.7%) were contrasted against children with sleep problems (1–10 points) (68.3%). At baseline, no significant differences was found between the groups on the CY-BOCS total score ($p = .872$). However, at post-treatment, children with sleeping problems had a higher score on the CY-BOCS total score ($p < .001$) and the between group effect size (Hedge's g) was 0.32 (95% CI 0.06–0.58) (Fig. 1). We investigated as well whether high score on individual sleep problems were associated with poorer treatment outcome, but the relationship was not significant in each case.

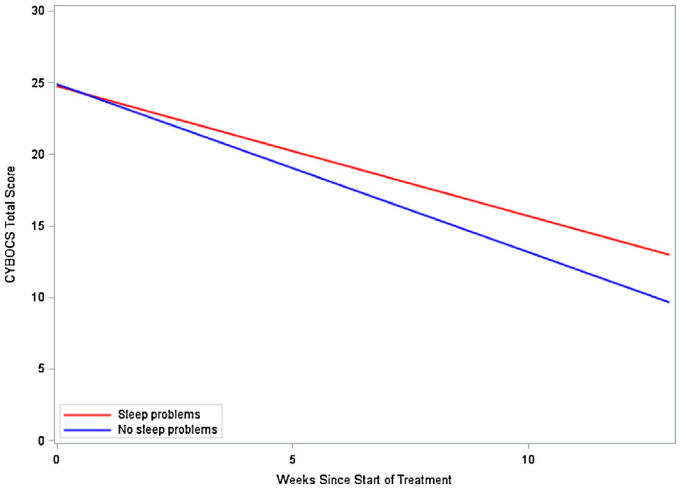

Fig. 1. Adjusted intent-to-treat CY-BOCS total score by weeks from baseline across sleep problem groups (sleep problems at baseline).

5. Discussion

This is, to our knowledge, the second study to report on how sleep problems in paediatric patients with OCD change following treatment with CBT. Like Storch et al. (2008) showed, sleep problems tend to decrease together with the OCD symptoms, so that, although two-thirds still had sleep problems, treatment responders have less sleep problems. Moreover, a new report from the CAMS researcher group shows similar results from the treatment with CBT on sleep problems in children and adolescents with "non-OCD" anxiety disorders (Caporino et al., 2014).

The resolution of sleep problems was not compromised by comorbid disorders, i.e. other anxiety disorders, ADHD, depression (a trend was found) or tics. It could indicate that the severity of those problems was alleviated by the resolution of OCD symptoms through the CBT. Moreover, our finding that OCD and comorbid ADHD was associated with a significant decrease in sleep problems was unexpected. These children had more sleep problem at baseline than OCD patients without ADHD, but the two groups did not differ at post-treatment. One could hypothesize that attention problems and sleep problems were causally related, possibly that elevated sleep problems could have led to ADHD-like symptoms that were tapped by the CBCL attention scale. However, an alternative hypothesis is regression towards the mean as the youth with comorbid OCD and ADHD started treatment with higher scored and thus the room to reduce the score was greater.

It was common in both CBT responders and non-responders to have some residual and mild/infrequent sleep problem. For those who had greater residual sleep problems, there was an increased risk for being non-responders with regard to the OCD-disorder as

well. However, it is not possible based on our data to decide the direction of causality, i.e. to say that having sleep problems that do not improve causes CBT to be less efficient. It may be that a lack of progress in the OCD-symptoms may cause continued sleep problems. However, it shows that the relationship needs to be studied using an experimental design.

We conclude that the decisive improvement of sleep problems in a majority of patients should be interpreted to mean that in most cases no treatment of the sleep disorder is necessary, even in cases with co-morbid disorders like those we investigated (i.e. depression, anxiety, ADHD and tics).

If it is clear that the sleep disorder is so severe that it is seen to compromise the CBT, or if the suffering entailed is marked, clinicians might evaluate the possibility of treatment for the sleep disorder, first in the form of bedtime fading (restriction of time in bed). Bedtime fading builds up sleep homeostatic pressure, thus, increasing the likelihood that one falls asleep and reduces the chances of long awakenings during the night (Paine & Gradisar, 2011). Such a study needs to be undertaken in OCD patients in the future. Moreover, we cannot exclude spontaneous improvement. Thus, a randomized controlled study, (e.g. CBT vs. wait-list) could strengthen our claim.

In the presence of sleep problems secondary to OCD, in situations where CBT does not relieve the OCD symptoms, one needs to consider the possibility of specific SRI (SSRI) treatment that may be efficient to ameliorate the sleep problems as well. However, there are currently no data that show this to be the case, even though data from the RUPP trial shows the principle to work in anxiety disorders (Alfano et al., 2007). Moreover, a new report from the CAMS researcher group (Caporino et al., 2014) shows that sertraline and sertraline plus CBT (for the anxiety disorder) was more effective than placebo in relieving sleep problems. The only study that, to our knowledge, could evaluate whether SSRI or the combination of SSRI and CBT could be helpful is the POTS Treatment Study Team (2004). It would be valuable if its database were re-evaluated in the same way. Similarly, an evaluation of CBT non-responders in our NordLOTS trial with regard to sleep problems is to be undertaken shortly.

In cases with sleep problems that do not respond to CBT or (S)SRI, it seems reasonable to treat the patient with a drug that is directed directly at the sleep disorder, such as melatonin. However, there is no evidence for its use in this situation, even though data show that it has a soporific effect when taken before bedtime (Smits et al., 2003) in children with primary insomnia. It is as well based on the positive clinical experience in child neuropsychiatric disorders like ADHD and Autism, where, moreover, some research evidence for efficacy and lack of toxicity is at hand (Cortese et al., 2013 Cortesi, Giannotti, Ivanenko, & Johnson, 2010). Moreover, in adolescent patients with OCD, whose circadian rhythm is out of alignment, a lower dose of melatonin taken in the late afternoon may restore the time pattern. This has been shown to work in teenagers with sleep-onset difficulties who had a circadian rythm misalignment (Eckerberg, Lowden, Nagai, & Akerstedt, 2012). Melatonin shows few adverse reactions (Smits et al., 2003) and the safety concerns for long-term use of melatonin seem positive (Hoebert, van der Heijden, van Geijlswijk, & Smits, 2009).

6. Limitations

The main limitation of our study is due to the measure used, i.e. the CBCL. Although used in many studies, the sleep items are not specific for the kind of sleep problems encountered in paediatric OCD, so there is a risk of a lack of ascertainment as well as overlap between some items. Future studies need to use sleep-specific scales (e.g. the use of Actigraphy, a parental report like the "Children's Sleep Habits Questionnaire", and a self-report as exemplified by the "Sleep self-report" (Owens, Maxim, Nobile, McGuinn, & Msall, 2000; Owens, Spirito, & McGuinn, 2000; Sadeh & Acebo, 2002), and procedures where observations of sleep problems in the lab (e.g. see Alfano and Kim, 2011) are used in parallel together with the appropriate interventions. A further limitation is that the yearly planned follow-up until 36 months are constrained to the use of the CBCL as sleep assessments, rather than those exemplified above.

Moreover, the NordLOTS step 1 is an uncontrolled study, although a large one, and consequently there is a risk that some improvement in sleep problems may be due to spontaneous improvement. Even though controlled studies (e.g. POTS Treatment Study Team, 2004) show that the placebo response of OCD symptoms is small to modest, this may not be the case with regard to sleep problems.

7. Conclusion

It is reasonable to interpret our findings that in patients with OCD in general, sleep problems associated with OCD gets better as the OCD symptoms respond to treatment. However, it is as well clear that a significant minority have continued sleep problems, and though this study does not prove it, it seems probable that the failure of CBT to bring relief to the OCD symptoms are associated with the failure with regard to the sleep problems. However, we cannot say based on our data anything about what causes what. Moreover, in cases with weak response to CBT, clinicians should alert themselves to their patient's sleep status, and attempt interventions within that area as well.

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